IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 10/508,978

Confirmation No. 4494

Applicant: Hwu et al.

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Commissioner for Patents
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DECLARATION UNDER 37 C.F.R. § 1.132 OF DR. J. WARREN LEONARD

1. I, Warren J. Leonard, M.D., am a co-inventor of the subject matter disclosed and claimed in the above-identified patent application.

2. Currently, I am Chief of the Laboratory of Molecular Immunology, Director of the Immunology Center, and Deputy Scientific Director of the National Heart, Lung, and Blood Institute of the National Institutes of Health. I received my Medical Degree from Stanford University in 1977 and have authored over 240 scientific articles during my career.

3. In an open-label, two-arm, phase I trial of human IL-21 for patients with malignant melanoma, patients received a recombinant human IL-21 molecule by intravenous bolus injection. See, Davis et al., *Clin. Cancer Research* 13(12): 3630-3636 (2007); a copy of which is attached hereto. Davis et al. report therein that the absolute number of natural killer (NK) cells decreased in the treated patients, whereas NK cell cytolytic activity in these

patients increased. See, the seventh sentence of the first complete paragraph of the left column on page 3635.

4. The decrease in the number of NK cells and the increase in NK cell cytolytic activity observed in humans, which were administered a recombinant human IL-21 molecule, reported by Davis et al. parallels the decrease in the number of NK cells (which was shown to be caused by apoptosis) and the increase in NK cell cytolytic activity observed in mice, which were administered a mouse IL-21 polynucleotide, which observations in mice are described in the specification of the above-identified application at paragraph [00132] of Example 7. Accordingly, the effect on NK cell number and NK cell cytolytic activity of a mouse IL-21 polynucleotide in a mouse was predictive of the effect on NK cell number and NK cell cytolytic activity of a human IL-21 molecule in a human.

5. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

2/12/08 2/14/08

Date: ~~2/12/07~~

Warren J. Leonard, M.D.

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